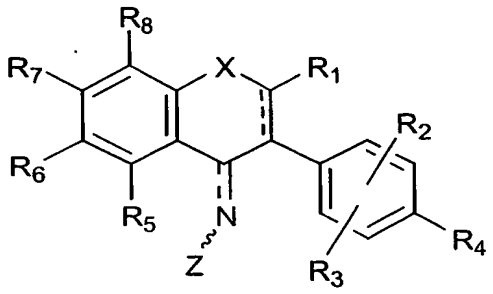
Claims

1. A compound of the general formula (I):



(I)

wherein

R_1, R_2, R_3, R_4, R_5, R_6, R_7 and R_8 are independently hydrogen, hydroxy, OR_9, OC(O)H, $OC(O)R_9$, $OS(O)R_9$, $OSi(R_{10})_3$, $C(O)R_{11}$, CO_2R_{12}, alkyl, haloalkyl, aryl, arylalkyl, thio, alkylthio, amino, alkylamino, dialkylamino, nitro or halo, or any two of the substituents R_2 R_3 and R_4 together with the carbon atoms to which they are attached form a cyclic alkyl, cyclic heteroalkyl, aryl or heteroaryl structure,

R_9 is alkyl, haloalkyl, aryl, arylalkyl or alkylaryl,

R_{10} is independently hydrogen, alkyl or aryl,

R_{11} is hydrogen, alkyl, aryl, arylalkyl, arylalkyl or an amino acid, and

R_{12} is hydrogen, alkyl, haloalkyl, aryl, arylalkyl or alkylaryl,

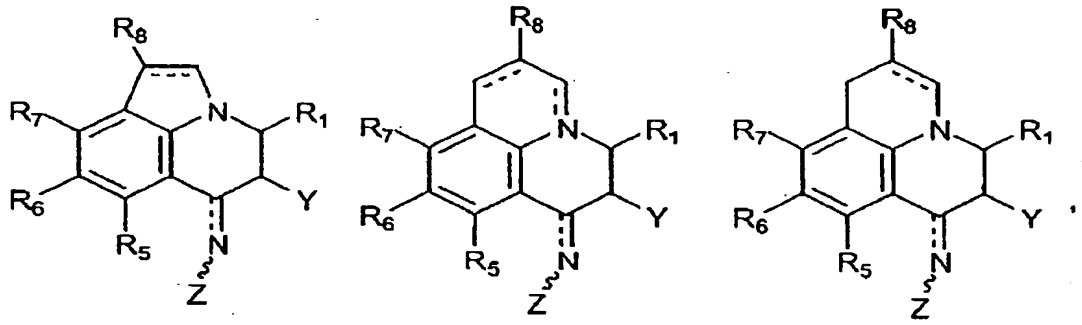
X is O, NR_{12} or S,

Z is R_{13}, $NR_{14}R_{15}$, $NR_{13}CONR_{14}R_{15}$, $N{=}CR_{16}R_{17}$ or OR_{13},

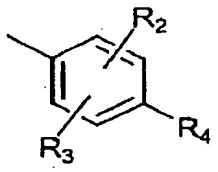
R_{13}, R_{14} and R_{15} are independently hydrogen, amino, thio, nitro, cyano, or optionally substituted alkyl, haloalkyl, acyl, aryl, heteroaryl, arylalkyl or alkylaryl, or the substituents R_{14} and R_{15} together with the nitrogen atom to which they are attached form an optionally substituted cyclic heteroalkyl or heteroaromatic structure, and

R_{16} and R_{17} are independently hydrogen, amino, thio, nitro, cyano, or optionally substituted alkyl, haloalkyl, acyl, aryl, heteroaryl, arylalkyl or alkylaryl, or the substituents R_{16} and R_{17} taken together with the carbon atom to which they are attached form an optionally substituted isoflavonoid ring system,

or when X is NR_{12}, the substituent R_{12} may be a bond such that R_8 and X together with the carbon atoms to which they are attached form one of the following structures:

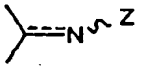
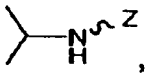


where Y is



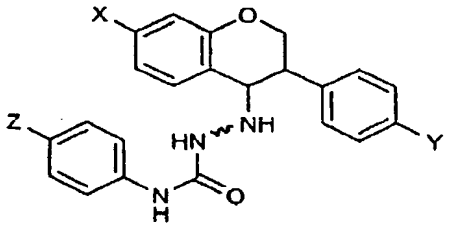
and wherein

R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and Z are as defined above, and

the drawing "---" represents either a single bond or a double bond and when it is a single bond, the drawing  represents  ,

which compounds include pharmaceutically acceptable salts and derivatives thereof

with the proviso that compounds of the formula



wherein

X is F or Cl,

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Y is H or F, and

Z is Cl, Br or CF_3

are specifically excluded, and

with the proviso that the following compounds

3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-amine

N-(3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-yl)-α-phenyl-benzeneacetamide

N-[3,4-Dihydro-3-(4-hydroxyphenyl)-2H-1-benzopyran-4-yl]-α-phenyl-benzeneacetamide

2,3-Dihydro-3-phenyl-4H-1-benzopyran-4-one oxime

2,3-Dihydro-3-phenyl-4H-1-benzopyran-4-one O-acetyloxime

N-[3-(3,4-Dimethoxyphenyl)-3,4-dihydro-7,8-dimethoxy-2H-1-benzopyran-4-yl]-formamide

2,3-Dihydro-2,3-diphenyl-4H-1-benzopyran-4-one hydrazone

4',7-Dimethoxy-isoflavanone oxime

3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-amine

N-(3-Phenyl-4-chromanyl)-acetamide

N-(7-Methoxy-3-phenyl-4-chromanyl)-acetamide

4',7-Dimethoxy-4-isoflavanamine

N-[7-Methoxy-3-(p-methoxyphenyl)-4-chromanyl]-acetamide

7-Methoxy-3-isoflavanamine

2'-Hydroxy-isoflavanone (2,4-dinitrophenyl)hydrazone

7-Methoxy-isoflavanone oxime

7-Methoxy-3',4'-(methylenedioxy)-isoflavanone (2,4-dinitrophenyl)hydrazone

7-Methoxy-isoflavanone phenylhydrazone

5,7-Dimethoxy-isoflavanone (2,4-dinitrophenyl)hydrazone

2,3-Dihydro-3-phenyl-4H-1-benzopyran-4-one oxime

Isoflavanone (2,4-dinitrophenyl)hydrazone

6-Hydroxy-isoflavanone (2,4-dinitrophenyl)hydrazone

7-Hydroxy-isoflavanone (2,4-dinitrophenyl)hydrazone

Isoflavanone semicarbazone

7-Methoxy-3',4'-(methylenedioxy)-isoflavanone (2,4-dinitrophenyl)hydrazone

7-Hydroxy-3',4'-(methylenedioxy)-isoflavanone (2,4-dinitrophenyl)hydrazone

7-Methoxy-isoflavanone (2,4-dinitrophenyl)hydrazone

7-Hydroxy-4'-methoxy-isoflavanone (2,4-dinitrophenyl)hydrazone

5,7-Dimethoxy-isoflavanone (2,4-dinitrophenyl)hydrazone

6-Methoxy-isoflavanone (2,4-dinitrophenyl)hydrazone

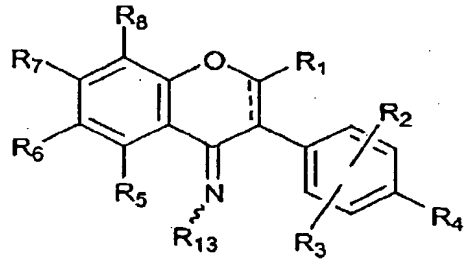
4',5,7-trimethoxy-isoflavanone (2,4-dinitrophenyl)hydrazone

7-Methoxy-2-methyl-isoflavanone (2,4-dinitrophenyl)hydrazone

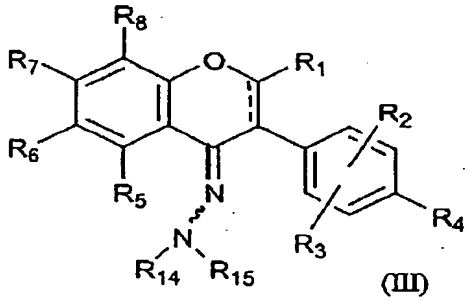
2-(Hydroxymethyl)-7-methoxy-isoflavanone (2,4-dinitrophenyl)hydrazone

and hydrochloride salts thereof are specifically excluded.

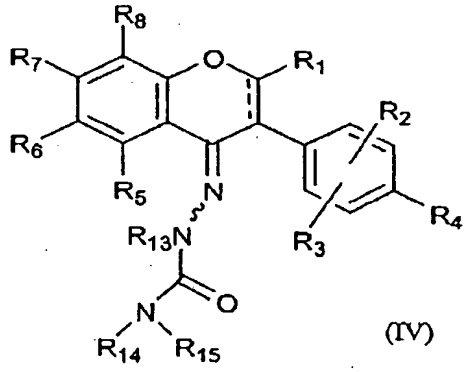
2. A compound according to claim 1, depicted by one of the general formulae (II)-(VIII):



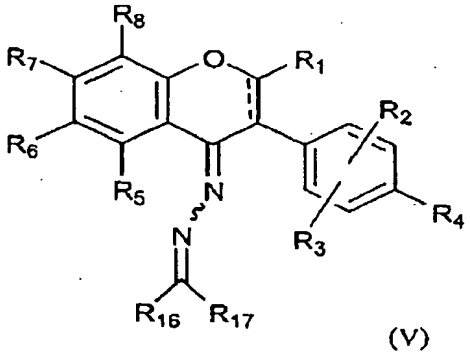
(II)



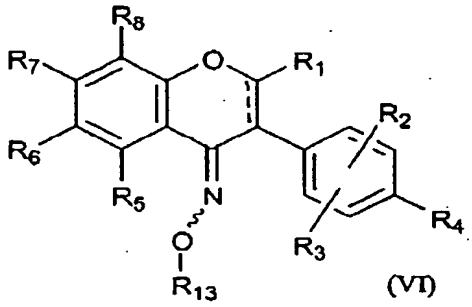
(III)



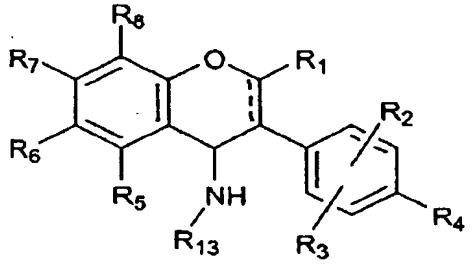
(IV)



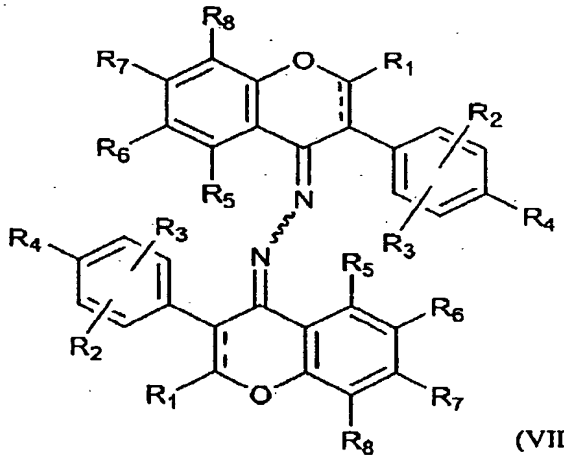
(V)



(VI)



(VII)



(VIII)

wherein

R_1, R_2, R_3, R_4, R_5, R_6, R_7 and R_8 are independently hydrogen, hydroxy, OR_9, $OC(O)R_9$, $OS(O)R_9$, alkyl, aryl, arylalkyl, thio, alkylthio, bromo, chloro or fluoro,

R_9 is alkyl, fluoroalkyl or arylalkyl,

R_{13}, R_{14} and R_{15} are independently hydrogen, amino, cyano, thio, nitro, or optionally substituted alkyl, haloalkyl, acyl, aryl, arylalkyl or alkylaryl, or the substituents R_{14} and R_{15} together with the nitrogen atom to which they are attached form an optionally substituted cyclic heteroalkyl or heteroaromatic structure,

R_{16} and R_{17} are independently hydrogen, amino, cyano, thio, nitro or optionally substituted alkyl, haloalkyl, acyl, aryl, arylalkyl or alkylaryl, or the substituents R_{16} and R_{17} taken together with the carbon atom to which they are attached form an optionally substituted isoflavonoid ring system, and

the drawing "---" represents either a single bond or a double bond.

3. A compound according to claim 2, wherein

R_1 is hydrogen,

R_2, R_3, R_5, R_6 and R_8 are independently hydrogen, hydroxy, OR_9, $OC(O)R_9$, alkyl, aryl or arylalkyl,

R_4 and R_7 are independently hydroxy, OR_9 or $OC(O)R_9$,

R_9 is methyl, ethyl, propyl, isopropyl or trifluoromethyl, and

R_{13}, R_{14} and R_{15} are independently hydrogen, methyl, ethyl, propyl, isopropyl, trifluoromethyl or optionally substituted phenyl, naphthyl or benzyl, or the substituents R_{14} and R_{15} together with the nitrogen atom to which they are attached form an optionally substituted cyclic heteroalkyl or heteroaromatic structure,

R_{16} and R_{17} are independently hydrogen, methyl, ethyl, propyl, isopropyl, trifluoromethyl or optionally substituted phenyl, naphthyl or benzyl, or the substituents R_{16} and R_{17} taken together with the carbon atom to which they are attached form an optionally substituted isoflavonoid ring system, and

the drawing "---" represents either a single bond or a double bond.

4. A compound according to claim 3, wherein

R_1 is hydrogen,

R_2, R_3, R_5, R_6 and R_8 are independently hydrogen, hydroxy, OR_9, $OC(O)R_9$ or methyl,

R_4 and R_7 are independently hydroxy, OR_9 or $OC(O)R_9$,

R_9 is methyl,

R_{13} is hydrogen, methyl, ethyl, trifluoromethyl, phenyl, chlorophenyl, nitrophenyl, toluyl, naphthyl, benzyl, chlorobenzyl, nitrobenzyl or methylbenzyl,

R_{14} is hydrogen and R_{15} is hydrogen, methyl, ethyl, trifluoromethyl, phenyl, chlorophenyl, nitrophenyl, toluyl, naphthyl, benzyl, chlorobenzyl, nitrobenzyl or methylbenzyl, or the substituents R_{14} and R_{15} together with the nitrogen atom to which they are attached form an optionally substituted cyclic heteroalkyl or heteroaromatic structure,

R_{16} and R_{17} are independently hydrogen, methyl, ethyl, trifluoromethyl, phenyl, chlorophenyl, nitrophenyl, toluyl, naphthyl, benzyl, chlorobenzyl, nitrobenzyl or methylbenzyl, or the substituents R_{16} and R_{17} taken together with the carbon atom to which they are attached form an optionally substituted isoflavonoid ring system, and the drawing "---" represents a single bond.

5. A compound according to claim 4 selected from compounds (1) - (14):

4',7-Dihydroxyisoflavanone (phenyl)hydrazone (1)
4',7-Dihydroxyisoflavanone (4-nitrophenyl)hydrazone (2)
4',7-Dihydroxyisoflavanone (4-methylphenyl)hydrazone (3)
4',7-Dihydroxyisoflavanone (benzyl)hydrazone (4)
4',7-Dihydroxyisoflavanone (4',7-dihydroxyisoflavanone)hydrazone (5)
4',7-Dihydroxyisoflavanone (2-chlorophenyl)hydrazone (6)
4',7-Dihydroxyisoflavanone (3-chlorophenyl)hydrazone (7)
4',7-Dihydroxyisoflavanone (4-chlorophenyl)hydrazone (8)
4',7-Dihydroxyisoflavanone (2-pyridyl)hydrazone (9)
4',7-Dihydroxyisoflavanone (4-cyanophenyl)hydrazone (10)
4',7-Dihydroxy-4-methylimino-isoflavan (11)
4',7-Dihydroxyisoflavanone oxime (12)
4-Amino-3',4'-dimethoxy-7-hydroxy-8-methylisoflavan (13)
N-[3',4'-dimethoxy-7-hydroxy-8-methyl-4-chromanyl)-acetamide (14)
which compounds include pharmaceutically acceptable salts thereof.

6. A process for the preparation of a compound of formula (I) as claimed in any one of claims 1 to 5 comprising the step of reacting the 4-keto group of a compound of the formula (X):

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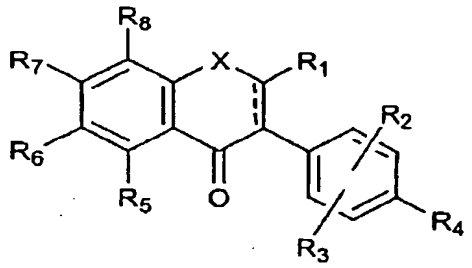

(X)

wherein

R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and X are as defined in claim 1, and the drawing "---" represents either a single bond or a double bond, with an aminating agent.

7. A method for the treatment, prophylaxis or amelioration of a disease or disorder which method includes the step of administering a therapeutically effective amount of one or more compounds of formula (I) or a pharmaceutically acceptable salt or derivative thereof to a subject,
with the proviso that the compounds and pharmaceutically acceptable salts of
3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-amine
N-(3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-yl)-α-phenyl-benzeneacetamide, and
N-[3,4-Dihydro-3-(4-hydroxyphenyl)-2H-1-benzopyran-4-yl]-α-phenyl-benzeneacetamide
are disclaimed for the treatment, prophylaxis or amelioration of atherosclerosis.

8. A method for the treatment, prevention or amelioration of diseases associated with aberrant cell survival, aberrant cell proliferation, abnormal cellular migration, abnormal angiogenesis, abnormal estrogen/androgen balance, dysfunctional or abnormal steroid genesis, degeneration including degenerative changes within blood vessel walls, inflammation, and immunological imbalance, which comprises administering to a subject one or more compounds of the formula (I) or a pharmaceutically acceptable salt or derivative thereof optionally in association with a carrier and/or excipient,
with the proviso that the compounds and pharmaceutically acceptable salts of
3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-amine
N-(3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-yl)-α-phenyl-benzeneacetamide, and

N-[3,4-Dihydro-3-(4-hydroxyphenyl)-2H-1-benzopyran-4-yl]-α-phenyl-benzeneacetamide are disclaimed for the treatment, prophylaxis or amelioration of atherosclerosis.

9. A method of inducing apoptosis in cells expressing abnormal prosurvival phenotype which comprises contacting said cells with one or more compounds of the formula (I) or a pharmaceutically acceptable salt or derivative thereof optionally in association with a carrier or excipient.

10. A method for inhibiting migration of cells having an abnormal cellular migration phenotype which comprises contacting said cells with a compound of the formula (I) or a pharmaceutically acceptable salt or derivative thereof optionally in association with a carrier or excipient.

11. A method for inhibiting angiogenesis in tissue expressing aberrant angiogenic phenotype which comprises contacting said tissue with a compound of the formula (I) or a pharmaceutically acceptable salt or derivative thereof optionally in association with a carrier or excipient,
with the proviso that the compounds and pharmaceutically acceptable salts of
3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-amine
N-(3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-yl)-α-phenyl-benzeneacetamide, and
N-[3,4-Dihydro-3-(4-hydroxyphenyl)-2H-1-benzopyran-4-yl]-α-phenyl-benzeneacetamide are disclaimed for the treatment, prophylaxis or amelioration of atherosclerosis.

12. A method for the treatment, prevention or amelioration of cancer in a mammal which method comprises the step of bringing a compound of formula (I) or a pharmaceutically acceptable salt or derivative thereof into contact with cancerous tissue in a mammal that is suffering from a tumour, such that neoplastic development in said cancerous tissue is retarded or arrested.

13. Use of one or more compounds of formula (I) or a pharmaceutically acceptable salt or derivative thereof in the manufacture of a medicament for the treatment of a disease or

disorder,
with the proviso that the compounds and pharmaceutically acceptable salts of
3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-amine
N-(3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-yl)-α-phenyl-benzeneacetamide, and
N-[3,4-Dihydro-3-(4-hydroxyphenyl)-2H-1-benzopyran-4-yl]-α-phenyl-benzeneacetamide
are disclaimed for the use in the manufacture of a medicament for the treatment, prophylaxis or amelioration of atherosclerosis.

14. Use of a compound of formula (I) or a pharmaceutically acceptable salt or derivative thereof as an anti-inflammatory agent.

15. An agent for the treatment, prophylaxis or amelioration of a disease or disorder, which agent comprises one or more compounds of formula (I) or a pharmaceutically acceptable salt or derivative thereof,
with the proviso that the compounds and pharmaceutically acceptable salts of
3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-amine
N-(3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-yl)-α-phenyl-benzeneacetamide, and
N-[3,4-Dihydro-3-(4-hydroxyphenyl)-2H-1-benzopyran-4-yl]-α-phenyl-benzeneacetamide
are disclaimed for the treatment, prophylaxis or amelioration of atherosclerosis.

16. A pharmaceutical composition which comprises one or more compounds of formula (I) or a pharmaceutically acceptable salt or derivative thereof in association with one or more pharmaceutical carriers, excipients, auxiliaries and/or diluents,
with the proviso that the compounds and pharmaceutically acceptable salts of
3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-amine
N-(3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-yl)-α-phenyl-benzeneacetamide, and
N-[3,4-Dihydro-3-(4-hydroxyphenyl)-2H-1-benzopyran-4-yl]-α-phenyl-benzeneacetamide
are disclaimed.

17. A drink or food-stuff, which contains one or more compounds of formula (I) or a pharmaceutically acceptable salt or derivative thereof.

18. A compound of formula (I) or a pharmaceutically acceptable salt thereof as herein described with reference to the Examples and/or accompanying drawings.